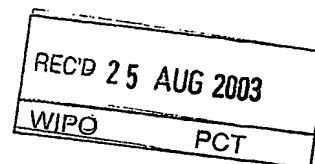


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Title: Method for converting venous blood values to arterial blood values,  
system for utilising said method and devices for such system.

IPC: -

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Patent- og Varemærkestyrelsen  
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higher than a reference condition (base excess (BE)) and the concentration of bicarbonate at a reference  $p\text{CO}_2$  (standard bicarbonate SBC). The variation in acid-base status between arterial and venous blood is due to oxygen removal from the blood and carbon dioxide addition due to metabolism at the tissues. In addition in patients with circulatory or  
5 metabolic abnormalities, the production of strong acid at the tissues due to anaerobic metabolism may also modify the acid-base status.

The acid-base status of arterial blood is used to assess the patients pulmonary and metabolic state. It has been argued (Adrogué et al., 1989a, 1989b; Brandt et al., 1995;  
10 Radiometer 1997) and to a large extent clinically accepted that venous blood samples are not adequate for assessing the acid/base and respiratory state of patients. This is thought to be particularly true for peripheral venous samples which *"are not recommended for blood gas analysis as they provide little or no information on the general status of the patient"* (Radiometer 1997).

15 In the intensive care unit placement of arterial catheters is routine practice and an assessment of the acid-base status can be obtained from the arterial blood. In some other hospital departments e.g. pulmonary medicine, or nephrology, arterial blood gases are also measured. However in other wards admitting acutely ill patients, e.g. cardiology,  
20 abdominal surgery, thoracic surgery and medicine, arterial samples are not usually taken. Usually a peripheral venous sample is taken and analysed in a central laboratory. The sample is usually taken aerobically, i.e. no attempt is made to ensure that  $p\text{O}_2$  and  $p\text{CO}_2$  remain constant during the sample procedure. Only a small amount of information concerning the acid-base status of the patient is measured in this sample i.e. the standard  
25 bicarbonate, SBC, and haemoglobin Hb. Other acid base parameters  $\text{pH}$ , carbon dioxide pressure ( $p\text{CO}_2$ ), base excess (BE), oxygen saturation ( $\text{SO}_2$ ) and oxygen pressure ( $p\text{O}_2$ ) are not measured, and if measured would probably not reflect the true values of venous blood at this sample site given the aerobic nature of the sample.

30 US 6,334,065 describes a pulse oximeter providing simultaneous and non-invasive oxygen status at multiple sites of a patient. The pulse oximeter described measures both arterial and venous oxygen saturation at any specific tissue site of the patient. It is mentioned that a corresponding computation of arterial minus venous oxygen saturation is advantageous for oxygen therapy patients. However, also as mentioned, the pulse oximeter is purely  
35 noninvasive in its way of functioning limiting the values capable of being derived.

US 3,874,850 describes an apparatus being an automatic blood sample analyzer for automatically measuring one or more unknown data or parameters of the blood samples. Based on the values measured, the apparatus comprises means for calculating a number

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of other parameters including acid-base status of the blood sample. The analyzer may also comprise means for photo-metrically measuring the hemoglobin contents of samples of blood. There is no computation of arterial blood values based on venous blood samples.

## 5 SUMMARY OF THE INVENTION

The object of the invention is to provide a method for performing the conversion of venous blood measurements to arterial values, including the design of a sampling tube for sampling anaerobic venous blood.

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This object is obtained by a method comprising the steps of:

- a) measuring or estimating, arterial oxygenation,
- b) measuring and estimating values of venous blood acid/base balance and oxygenation status of a venous blood sample taken anerobically,
- 15 - c) converting the venous blood values by applying a mathematical model for estimating and/or calculating blood acid/base balance and oxygenation status into estimated arterial blood values.

The object may also be obtained by a method comprising the steps of:

- 20 - b) measuring and estimating values of venous blood acid/base balance and oxygenation status of a venous blood sample taken anerobically,
- a) measuring or estimating, arterial oxygenation,
- c) converting the venous blood values by applying a mathematical model for estimating and/or calculating blood acid/base balance and oxygenation status into estimated arterial
- 25 blood values.

By means of mathematical models for the acid-base balance of the body, venous blood sample values of acid-base balance and of oxygen status together with pulse oximetry may be used to convert the venous blood values to corresponding arterial values.

30

- We argue that parameters describing the venous acid-base chemistry should be measured, and describe a method whereby venous values can be combined with a determination of arterial oxygen saturation with a pulse oximeter to calculate predictions ( $SBC_{ap}$ ,  $pH_{ap}$ ,  $pCO_{2ap}$ ,  $BE_{ap}$  and  $SO_{2ap}$ ) of the corresponding arterial values, ( $SBC_a$ ,  $pH_a$ ,  $pCO_{2a}$ ,  $BE_a$  and
- 35  $SO_{2a}$ ). This implies that the acid/base and respiratory status can be assessed without taking an arterial blood sample. To do so requires anaerobic sampling of the venous blood and this patent also describes the design of a sampling bottle for this purpose. This method will make acid/base and respiratory status available in a large number of patients without the cost, risk and inconvenience of taking an arterial sample, in particular in

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departments where arterial samples traditionally are only taken rarely. Having the acid/base and respiratory status available will make it easier to diagnose different types of respiratory and metabolic acidosis or alkalosis.

- 5 The assumptions of the models comprise that no acid is added between the arterial blood and the venous blood drawn, i.e. no anaerobic metabolism is taking place in the intermediate organ or tissue. It is known that this is not the case for haemo-dynamically unstable patients and for patients with severe chronic suffering.
- 10 The potential for use of venous blood samples to assess the status of acutely ill patients in various hospital departments is illustrated in figure 1 which graphically shows the acute blood samples in different patient groups at Aalborg Hospital in Denmark in 1999. Light bars indicate arterial blood samples, dark bars indicate venous blood samples. Three different types of department can be identified within those treating acutely ill patients. In
- 15 the first group arterial blood samples are taken frequently (70,000 per year at Aalborg Hospital, Denmark) and often analysed at the point of care. This group includes intensive care units, departments of anaesthesia and trauma units. In the second group arterial blood samples are taken regularly (2,000 arterial blood samples per year at Aalborg Hospital, Denmark). This group includes the departments of pulmonary medicine and
- 20 nephrology. In the third group arterial blood samples are taken occasionally. This group includes for example departments of cardiology, abdominal surgery, thoracic surgery and medicine.

- In the departments of groups 2 and 3 venous blood samples are taken much more
- 25 frequently than arterial samples. Indeed, when taken in total, the number of venous blood samples taken in acutely ill patients actually exceeds the number of arterial blood samples (figure 1). It is in these departments that venous samples are usually analysed in the central laboratory where measurements of standard bicarbonate (SBC), total haemoglobin (Hb), and other blood values are taken, without a full blood gas analysis.

- 30 In order to test the strength and validity of the models it is therefore necessary to test the models for different groups of patients with varying haemo-dynamic conditions and accordingly different  $O_2$  and  $CO_2$  conversion in the tissues. Furthermore it has to be proven that the models may use venous values irrespective of the location where the venous
- 35 blood sample is drawn such as a central venous catheter or a Swan Ganz catheter or from a peripheral vein.

Input for the mathematical models are venous values together with information of the arterial oxygenation as measured by means of as example a pulse oximeter.

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In order to verify the validity of the models for converting venous blood sample values to arterial values the corresponding arterial values derived may be compared to an arterial blood sample drawn simultaneously with drawing of the venous blood sample.

5

#### DESCRIPTION OF THE INVENTION

This section will be described in four parts. In part 1 the invention will be described with reference to the accompanying fig. 2 schematically showing a method for performing the  
10 prediction of arterial values from a venous blood sample.

In part 2 a design for a sampling bottle, capable of being used for anaerobic sampling of venous blood, is described. Anaerobic venous samples being required for the method described in step 1.

15

In part 3 two patient cases are described, both illustrating the potential use of the method. The first patient had a metabolic alkalosis due to potassium deficiency. In that patient a venous blood sample converted to arterial values would have revealed this problem before it developed into a crisis. The second example is a postoperative patient, where an arterial  
20 sample was actually available. This case is included to show that the information that can be derived from a venous sample converted into arterial values is equivalent to the information derived from the arterial sample. The case also shows that conversion of venous blood to arterial values is necessary: the calculated arterial values showed that arterial  $pCO_2$  was normal, despite the high venous value.

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In section 4 it is shown that arterial values, calculated from the method of converting venous to arterial values, compare well with measured arterial values in 69 patient cases, including some categories of very ill patients. The accuracy of the converted venous values does not match what is obtained from an arterial sample, but is clearly sufficient for a  
30 clinical judgement to be made. As a minimum the arterialization method can be seen as a quite accurate screening method, that indicates when an arterial sample should be taken.

#### 1. Conversion of venous blood values to arterial blood

35 The invention will be described with reference to the accompanying fig. 2 schematically showing a method for performing the prediction of arterial blood acid-base status values from an anaerobically sampled venous blood sample.

Arterial blood gasses are, as an example, estimated as given in the 4 steps below.

Step 1: An anaerobic venous blood sample is drawn and analysed using standard blood  
5 gas analysis technology (e.g. Radiometer, 1994) to provide a picture of the acid/base status of the venous blood ( $SBC_v$ ,  $pH_v$ ,  $pCO_{2v}$ ,  $BE_v$  and  $SO_{2v}$ ).

Step 2: The arterial oxygen saturation is estimated or measured non-invasively, possibly  
by pulse oximetry.

10

Step 3: For a blood sample passing through the tissues from the arteries into the veins, the ratio of the amount of  $CO_2$  added (i.e. the rate of  $CO_2$  production ( $VCO_2$ )) and  $O_2$  removed (i.e. the rate of  $O_2$  utilisation ( $VO_2$ )), due to aerobic metabolism is defined as the respiratory quotient ( $RQ = VCO_2/VO_2$ ).  $RQ$  is often approximated by measurement of  
15 inspiratory and expiratory gases taken at the mouth, through the measurement of inspiratory oxygen ( $FI O_2$ ) and carbon dioxide ( $FI CO_2$ ) fraction and either end tidal fractions of oxygen ( $Fe'O_2$ ) and carbon dioxide ( $Fe'CO_2$ ) or mixed expired fractions of oxygen ( $FeO_2$ ) and carbon dioxide ( $FeCO_2$ ) using the equations:

$$20 \quad RQ = \frac{Fe'CO_2 - FI CO_2}{FI O_2 - Fe'O_2} \quad \text{or} \quad RQ = \frac{FeCO_2 - FI CO_2}{FI O_2 - FeO_2}$$

Approximation of  $RQ$  by this method often gives values which can vary substantially.

However, the true value of  $RQ$  at the tissues can only vary between 0.7-1.0, being 0.7 in  
25 aerobic metabolism of fat and 1.0 in aerobic metabolism of carbohydrate. In this step a mathematical model of blood acid/base and oxygenation status (e.g. Rees et al, 1996, 1997, etc) is used to perform a simulation, where  $O_2$  is added and  $CO_2$  removed from the venous blood in a ratio determined by a constant respiratory quotient, set to be within the physiologically possible range 0.7-1.0. This simulation is performed until the simulated  
30 oxygen saturation is equal to that estimated or measured in step 2, i.e. that in arterial blood.

Step 4: The model of blood acid/base and oxygenation status is then used to calculate a picture of the acid/base status and the oxygenation of the arterial blood ( $SBC_{ap}$ ,  $pH_{ap}$ ,  
35  $pCO_{2ap}$ ,  $BE_{ap}$  and  $SO_{2ap}$ ). This is possible as the simulated removal of  $CO_2$  and  $O_2$  from venous blood at a fixed  $RQ$  ensures that when the simulated arterial oxygenation matches that measured, then the simulated values of other arterial acid-base variables should also match those measured.

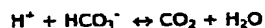
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For the purpose of testing the venous to arterial conversion method the predictions of arterial acid base status ( $SBC_{ap}$ ,  $pH_{ap}$ ,  $pCO_{2ap}$ ,  $BE_{ap}$  and  $SO_{2ap}$ ) obtained from the method can be compared against those measured ( $SBC_a$ ,  $pH_a$ ,  $pCO_{2a}$ ,  $BE_a$  and  $SO_{2a}$ ), examples of which are given in sections 3 and 4.

5

The fundamental assumption contained in this method is that a constant value of RQ may be used to perform the venous arterial conversion. This requires that little or no anaerobic metabolism occurs across the tissue where the venous blood sample is taken. If anaerobic metabolism were present the strong acid produced by this process ( $H^+$ ) would bind with

10 bicarbonate ( $HCO_3^-$ ) in the blood to form  $CO_2$  in the following reversible reaction



The increase in  $CO_2$  production by this reaction would mean that the apparent  $VCO_2$  would  
15 be increased without an increase in  $VO_2$ , and hence RQ would increase. The degree of anaerobic metabolism depends upon the circulatory and metabolic state of the patient. In a normal well perfused peripheral limb it is unlikely that anaerobic metabolism occurs. The quality of perfusion of a limb can be assessed clinically by the presence of a clearly recognizable arterial pulse determined by palpation, a normal capillary response, and a  
20 normal color and temperature of the limb. Central or mixed venous blood is a mixture of blood from several sites and may therefore contain blood from an area of the body with anaerobic metabolism. The selection of the sample site is therefore important. In section 3 the validity of the method is tested for peripheral venous blood sampled from a clinically considered well perfused arm by comparing arterial values derived using the method with  
25 those obtained from an arterial blood sample drawn simultaneously with the drawing of the venous sample.

2. Design of a sampling bottle, capable of being used for anaerobic sampling of venous blood.

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The method of converting venous values describing the acid-base status of the blood to arterial values only applies if the venous blood samples are taken anaerobically, i.e. it is ensured that the  $O_2$  and  $CO_2$  pressure in the sample remains constant during and after the sampling procedure.

35

Currently, it is normal practice that only arterial samples are taken anaerobically. These are usually taken via a sampling syringe from a sampling connector (A) at the sampling site of an arterial catheter, cannula or needle, as illustrated in figure 3. Arterial sampling syringes (e.g. with reference to a normal PICCO syringe to come) are heparinized to

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prevent coagulation of the sample. After sampling of the blood the syringe is usually placed in a verticle position with the open end (B) (figure 3) uppermost, agitated and trapped air expelled using the plunger (C). This is only possible because the syringe is open to the environment, a lid being placed on the syringe only after expulsion of trapped  
5 air.

In principle, venous blood sampled using arterial sampling syringes could be used in the method of converting venous to arterial values described here. However, the use of open syringes increases the risk of infection of the person handling the blood. In departments  
10 routinely taking venous blood to assess the status of acutely admitted patients, venous blood samples are not usually taken using open syringes. Instead venous blood samples are taken using the sampling method illustrated in figure 4. A venous sampling connector (A) is attached to the venous sampling site. The connector includes a needle (D), covered with rubber so as to prevent leakage of blood except when pressure is applied to the  
15 rubber to expose the needle. The venous sampling bottle is sealed with a sealing membrane (E). Blood cannot enter or leave the bottle until the bottle is pressed onto the sampling connector. At this point the needle is exposed, pierces the sealing membrane, and a blood sample may be taken. Different sampling bottles often contain chemicals for specific conservation or anaysis of the blood depending upon the parameters to be  
20 measured e.g. electrolytes, coagulation etc. However these sampling bottles also contain oxygen and/or carbon dioxide (typically air), which may diffuse into the blood sample altering its acid base status. In addition, since the sample bottle is closed there is no means to expel air which may enter the bottle during the sampling procedure.

25 Figure 5 illustrates an example of the invention according to claims 17-20 i.e. the design of a sample bottle suitable for anaerobic sampling of venous blood.

The example design illustrates a sample bottle (B) with two heparinized chambers B1 and B2. Initially the two chambers are joined, as illustrated in figure 5a. The complete bottle is  
30 then pressed on the sampling connector (A) and the plunger used to draw blood, and possibly air into both compartments. The sample bottle is then detached from the sampling connector as illustrated in figure 5b and placed vertically with the plunger facing uppermost. By agitating the bottle and withdrawing the plunger further, any air in chamber B1 is drawn into chamber B2. The two chambers B1 and B2 are then separated.  
35 The rubber seals on the sampling needle (C) and the sealing membrane (D) ensure no leakage of blood. Chamber B1 contains only anaerobic venous blood, analysis of which may then be used in the arterial conversion algorithm. Chamber B2 contains air and blood and may be discarded.



The amount of air in the chambers can be further reduced by applying a partial or complete vacuum within the sample bottle prior to sampling. In addition if the initial gas in the sampling bottle contains inert gasses, or  $O_2$  and  $CO_2$  adjusted to typical venous values, then the effects of any residual gasses in the sampling bottle will be minimised.

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3. Clinical cases illustrating the potential use of the venous to arterial conversion method

This section describes two patient examples, the first with a metabolic alkalosis due to potassium deficiency. In this patient a venous blood sample converted to an arterial value  
10 would have revealed the problem before it developed into a crisis. The second example is a postoperative patient, where an arterial sample was actually available. This case is included to show that the information that can be derived from an venous sample converted to arterial values is equivalent to the information derived from the arterial sample. The case also shows that conversion of venous values to arterial values is  
15 necessary: the converted venous values show that arterial  $pCO_2$  is normal, despite the high venous value.

Case 1- Metabolic alkalosis due to potassium deficiency

A patient, age 60, male, was acutely admitted to the surgical department complaining of  
20 abdominal pain, and having vomited repeatedly over the past week. A peripheral venous sample was taken and analysed routinely, without a blood gas analysis, giving a high standard bicarbonate  $SBC_v = 38$  mmol/l, a normal haemoglobin  $Hb_v = 7.0$  mmol/l, and a potassium value at the low end of the normal range  $K_v = 3.6$  mmol/l. The high SBC caused by loss of acid and potassium due to vomiting remained unnoticed for 3 days, at which  
25 point the patients respiratory drive and cardiac function had deteriorated to the point of pulmonary odema, and an arterial blood gas was taken. Arterial blood gas values ( $pH_a = 7.60$ ,  $BE_a = 18$  mmol/l,  $pCO_{2,a} = 6.0$  kPa,  $SO_{2,a} = 0.92$ ) showed very severe metabolic alkalosis. The patient was then transferred to the intensive care unit, where treatment for this metabolic alkalosis proceeded for approximately two weeks.

30

For this patient, analysis of the peripheral venous blood gases on admission might have highlighted the severe alkalosis. In current clinical practice analysis of the peripheral venous blood gases are not generally accepted (Radiometer 1997). Conversion of the venous blood gas values to arterial values using the method included here might then both  
35 have highlighted the severe alkalosis before the patient reached a critical state, and given a clinically acceptable picture of the patient.

#### Case 2 – Post-operative coronary artery bypass patient

- A patient, age 64, male, presented in the post operative intensive care unit following coronary artery bypass surgery. During the post operative period the patient was haemodynamically stable. An arterial catheter was present in this patient and simultaneous
- 5 samples of arterial and peripheral venous blood were taken and analysed for blood gases. Venous blood values were  $SBC_v = 23.7$  mmol/l,  $pH_v = 7.29$ ,  $pCO_{2,v} = 7.20$  kPa,  $BE_v = -0.3$  mmol/l and  $SO_{2,v} = 0.36$ . If interpreted directly these values would suggest that the patient had a respiratory abnormality causing a high  $pCO_{2,v}$ . However, when the venous to arterial conversion method was used to calculate arterial blood gas values a relatively
- 10 normal pattern presented  $SBC_{ap} = 22.9$  mmol/l,  $pH_{ap} = 7.35$ ,  $pCO_{2,ap} = 5.82$  kPa,  $BE_{ap} = -1.8$  mmol/l and  $SO_{2,ap} = 0.98$  suggesting that the patient did not have a respiratory abnormality. These converted venous values gave the same clinical picture as arterial values measured for comparison ( $SBC_a = 23.6$  mmol/l,  $pH_a = 7.37$ ,  $pCO_{2,a} = 5.54$  kPa,  $BE_a = -1.1$  mmol/l, and  $SO_{2,a} = 0.98$ ), which were also within the normal range. The
- 15 Information derived from the converted venous sample was therefore clinically equivalent to the information derived from the arterial sample. In this case an interpretation of the patient state could not be made from the venous blood without a conversion to arterial values since the converted values showed that arterial  $pCO_2$  was normal, despite the high venous value. If this patient had presented at the ward, without an arterial catheter
- 20 conversion of venous blood to arterial values would have been necessary to obtain the correct clinical interpretation.

#### 4. Conversion of venous blood values to arterial values in 69 clinical cases

- 25 This section describes the results of using the method for conversion of venous to arterial values. Peripheral venous blood samples were taken in 69 cases, and used to measure  $SBC_v$ ,  $pH_v$ ,  $pCO_{2,v}$ ,  $BE_v$  and  $SO_{2,v}$ . The method was then used to predict arterial blood values  $SBC_{ap}$ ,  $pH_{ap}$ ,  $pCO_{2,ap}$ ,  $BE_{ap}$  and  $SO_{2,ap}$ . These arterial predictions were then compared with measurements of arterial blood  $SBC_a$ ,  $pH_a$ ,  $pCO_{2,a}$ ,  $BE_a$  and  $SO_{2,a}$  taken simultaneously
- 30 with the venous samples. Section 4.1 describes the patient groups included in this study including their severity of metabolic and respiratory disorders. Section 4.2 describes the results of the venous to arterial conversion method. In this section each predicted variable ( $SBC_{ap}$ ,  $pH_{ap}$ ,  $pCO_{2,ap}$ ,  $BE_{ap}$  and  $SO_{2,ap}$ ) is compared in turn to measured arterial values, and the accuracy and precision of the prediction quantified.

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##### 4.1 Study population

Patients were studied from the following groups a) post operative coronary artery bypass patients, both haemodynamically stable and unstable; b) patients with sepsis, both

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haemodynamically stable and unstable; and d) Patients with chronic obstructive lung disease, both mechanically ventilated and spontaneously breathing. These groups were selected to represent a range of acid base status including metabolic and respiratory abnormalities, and presented with the values (median, range)  $pH_a = 7.40$ , 7.24 to 7.54;  $BE_s = 0.6$  mmol/l, -6.9 to 19.7 mmol/l;  $SBC_s = 25.0$  mmol/l, 18.8 to 44.3 mmol/l;  $pCO_{2,a} = 5.68$  kPa, 4.0 to 10.8 kPa. Patients also presented with a broad range of arterio-venous oxygen saturation difference (median, range) 0.15, 0.00 to 0.74. Arterial and peripheral venous blood samples were taken simultaneously with peripheral samples being taken from what were clinically considered well perfused arms. Results of these groups are presented here pooled.

#### 4.2 Results

In this section we present a comparison of arterial values predicted using the venous to arterial conversion method ( $SBC_{ap}$ ,  $pH_{ap}$ ,  $pCO_{2,ap}$ ,  $BE_{ap}$  and  $SO_{2,ap}$ ) with measured arterial values ( $SBC_a$ ,  $pH_a$ ,  $pCO_{2,a}$ ,  $BE_s$  and  $SO_{2,a}$ ).

##### $pCO_{2,a}$ versus $pCO_{2,ap}$

Figure 6 illustrates a Bland-Altman plot of measured arterial carbon dioxide pressure  $pCO_2$  ( $pCO_{2,a}$ ) versus that predicted using the venous to arterial conversion method ( $pCO_{2,ap}$ ). The prediction of  $pCO_{2,ap}$  can be seen as both accurate and precise ( $pCO_{2,a} - pCO_{2,ap} = -0.10 \pm 0.32$  kPa). In addition, errors in the prediction of  $pCO_{2,ap}$  are clinically unimportant when compared to the size of the arterial - venous  $pCO_2$  difference  $pCO_{2,a} - pCO_{2,v} = -0.64 \pm 0.63$  kPa.

##### $SBC_s$ versus $SBC_{ap}$

Figure 7 illustrates a Bland-Altman plot of measured arterial Standard Bicarbonate  $SBC$  ( $SBC_a$ ) versus that predicted using the venous to arterial conversion method ( $SBC_{ap}$ ). The prediction of  $SBC_{ap}$  can be seen as both accurate and precise ( $SBC_a - SBC_{ap} = 0.17 \pm 0.5$  mmol/l). Since  $SBC$  changes with the addition of acid, the small bias of 0.17 mmol/l is equivalent to the finding that the base excess changes by about 0.2 mmol/l as the blood flows through the tissues.

##### $ABE_s$ versus $ABE_{ap}$

The major assumption in the venous to arterial conversion method is that no significant amount of strong acid is added to the blood as it passes through the tissues across which

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the arterial and venous blood samples are taken. To verify this, figure 8 illustrates a Bland-Altman plot of measured arterial Base Excess BE ( $BE_a$ ) against that predicted from the arterial to venous conversion method ( $BE_{ap}$ ).  $BE_a - BE_{ap} = 0.2 \pm 0.5$  mmol/l. This implies that  $0.2 \pm 0.5$  mmol/l acid is added when the blood is passing through the tissues i.e an insignificant amount.

$pH_a$  versus  $pH_{ap}$

Figure 9 illustrates a Bland-Altman plot of measured arterial pH ( $pH_a$ ) versus that predicted using the venous to arterial conversion method ( $pH_{ap}$ ). The prediction of  $pH_{ap}$  can be seen as both accurate and precise ( $pH_a - pH_{ap} = 0.008 \pm 0.013$ ).

Possible groups of patients suitable for the invention.

- 15 The patient groups presented in section 4 reflect the testing of the method where simultaneous sampling of arterial blood is necessary for comparison with the those calculated by the method. When applying the method arterial samples would not be taken. The method may therefore be applied in all: normal subjects, patients, or animals in which a venous sample can be taken in combination with a measurement of arterial oxygenation, usually performed using a pulse oximeter. Whilst the method is tested here for the sampling of peripheral venous blood the method may also be applied to the sampling of central or mixed venous blood.

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CLAIMS

1. A method of converting venous blood values to arterial blood values, said method comprising the steps of:
  - 5 - a) measuring or estimating, arterial oxygenation,
  - b) measuring and estimating values of venous blood acid/base balance and oxygenation status of a venous blood sample,
  - c) converting the venous blood values by applying a mathematical model for estimating and/or calculating blood acid/base balance and oxygenation status into estimated arterial
  - 10 blood values.
2. A method of converting venous blood values to arterial blood values, said method comprising the steps of:
  - b) measuring and estimating values of venous blood acid/base balance and oxygenation
  - 15 status of a venous blood sample,
  - a) measuring or estimating, arterial oxygenation,
  - c) converting the venous blood values by applying a mathematical model for estimating and/or calculating blood acid/base balance and oxygenation status into estimated arterial blood values.
  - 20
3. A method according to claim 1 or claim 2, said measuring and analyzing comprising the steps of:
  - d) drawing an anaerobic venous blood sample,
  - e) analysing said anaerobic venous blood sample for evaluating the acid/base balance of
  - 25 the venous blood sample, and
  - f) analysing said anaerobic venous blood sample for evaluating the oxygenation status of the venous blood sample.
4. A method according to claim 1 or claim 2, said measuring and analyzing comprising the
- 30 steps of:
  - d) drawing an anaerobic venous blood sample,
  - f) analysing said anaerobic venous blood sample for evaluating the oxygenation status of the venous blood sample, and
  - g) analysing said anaerobic venous blood sample for evaluating the acid/base status of
  - 35 the venous blood sample.

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5. A method according to any of the preceding claims, said method comprising the further step of
- g) measuring or estimating the arterial oxygenation (i.e. oxygen saturation, pressure or concentration) by applying any suitable means for such measuring or estimation, said
- 5 further step being performed at any time in relation to any of the steps of claims 1-3.
6. A method according to claim 5, said method comprising the even further step of
- h) simulating the blood acid/base balance and oxygenation status of an arterial blood sample by use of mathematical modelling.
- 10
7. A method according to claim 6, said method comprising still even further steps of
- i) mathematical modelling comprising simulated addition of oxygen ( $O_2$ ) to and removal of carbon dioxide ( $CO_2$ ) from the venous blood sample values in a ratio determined by the respiratory quotient,
- 15 - j) said mathematical modelling being performed until the simulated oxygen level is equal to the arterial oxygenation level measured or estimated, and
- k) calculating or estimating the acid/base status and the oxygenation of the arterial blood by applying the result of said modelling.
- 20
8. A method according to any of the claims 1-4, said method comprising a further step of
- l) measuring or estimating the arterial carbon dioxide level (i.e. carbon dioxide pressure, total concentration or bicarbonate concentration) by applying any suitable means for such measuring or estimation, said further step being performed at any time in relation to any of the steps of claims 1-4.
- 25
9. A method according to claim 8, said method comprising an even further step of
- m) simulating the blood acid/base balance and oxygenation status of arterial blood sample by use of modelling.
- 30
10. A method according to claim 9, said method comprising the still even further steps of
- n) mathematical modelling comprising simulated addition of  $O_2$  to and removing  $CO_2$  from the venous blood sample values in a ratio determined by the respiratory quotient,
  - o) said modelling being performed until the simulated carbon dioxide level is equal to the arterial carbon dioxide level measured or estimated, and
- 35 - p) calculating or estimating the acid/base balance and the oxygenation of the arterial blood by applying the result of said modelling.
11. A method according to any of the claims 3-7, where the measuring or estimating of the arterial oxygen saturation is done by pulse oximetry.

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12. A system utilizing the method according to any of the preceding claims, said system comprising a blood gas analyzer, said analyzer capable of providing calculated or estimated arterial blood acid/base status and oxygenation from a venous blood sample.
- 5
13. A system according to claim 12, said system comprising means for measuring arterial oxygenation saturation, where the means preferably is a pulse oximeter
14. A system according to claim 12 or claim 14, said system comprising a device for
- 10 anaerobic sampling, preferably by drawing of a venous blood sample.
15. A system comprising a computer or a medical device for running the modelling according to claim 1 and any of claims 3-11, and said computer or medical device comprising one or more hardware components chosen among: blood gas analyzer and
- 15 pulse oximeter.
16. A system comprising a computer or a medical device for running the modelling according to claim 2 and any of claims 3-11, and said computer or medical device comprising one or more hardware components chosen among: blood gas analyzer and
- 20 pulse oximeter.
17. A device for anaerobic drawing of venous blood, said device capable of reducing any residual gases in a blood sample bottle by applying a partial or complete vacuum within the sample bottle.
- 25
18. A device for anaerobic drawing of venous blood, said device capable of reducing the effects of any residual gases in a blood sample bottle by using gases with partial O<sub>2</sub> and CO<sub>2</sub> pressures adapted to typical venous values within the sample bottle.
- 30 19. A device for anaerobic drawing of venous blood, said device capable of reducing the effects of any residual gases in a blood sample bottle by using one or more inert gases in the sample bottle.
20. A device for anaerobic drawing of blood venous blood, said device capable of reducing
- 35 any residual gases in a blood sample by dividing the sample bottle into one or more compartments with at least one compartment containing blood only.

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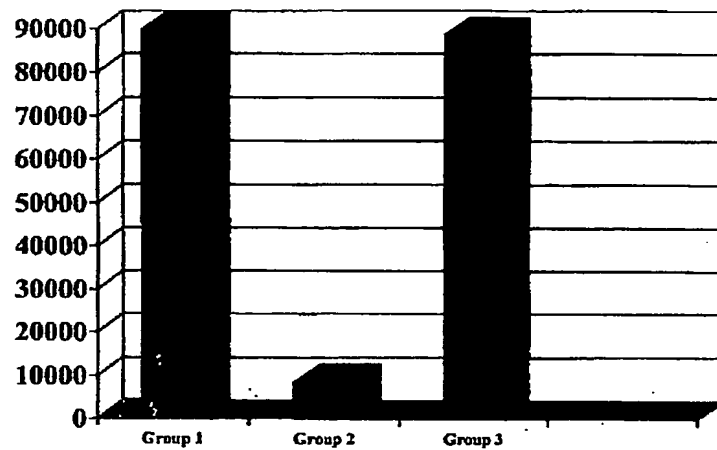


Fig. 1

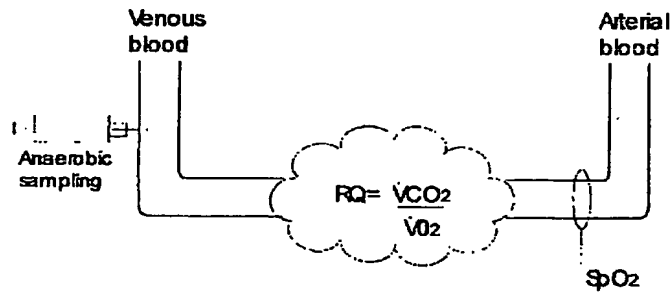


Fig. 2

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Fig. 3

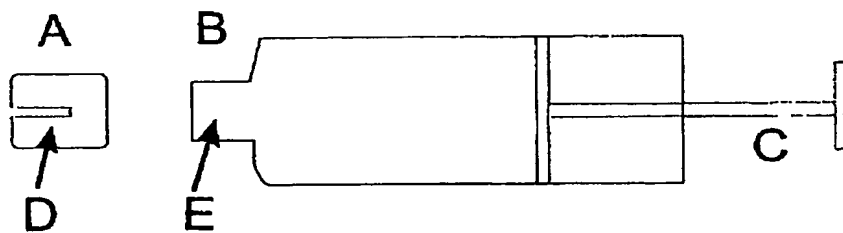


Fig. 4

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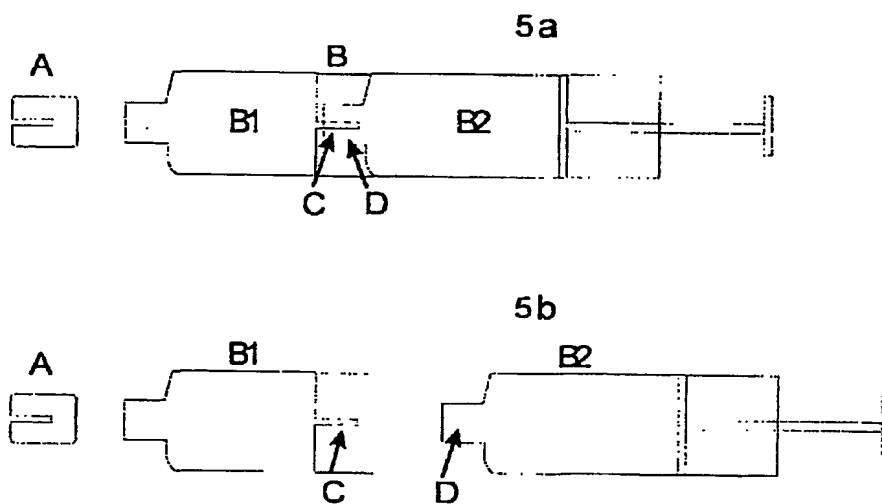


Fig. 5

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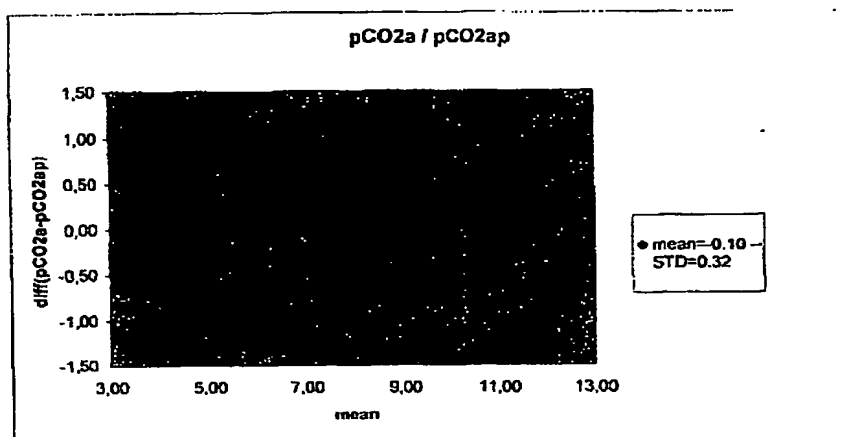


Fig. 6

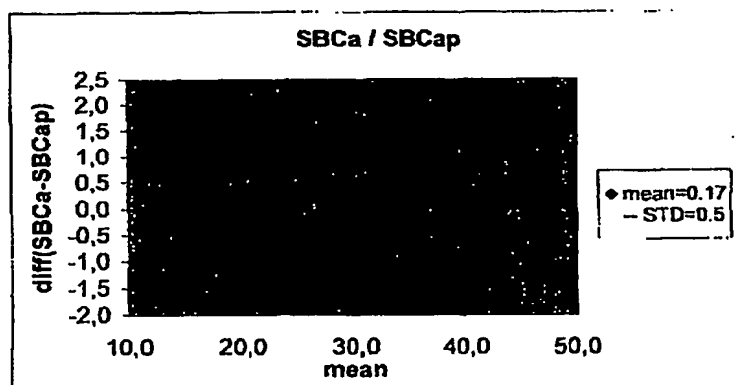


Fig. 7

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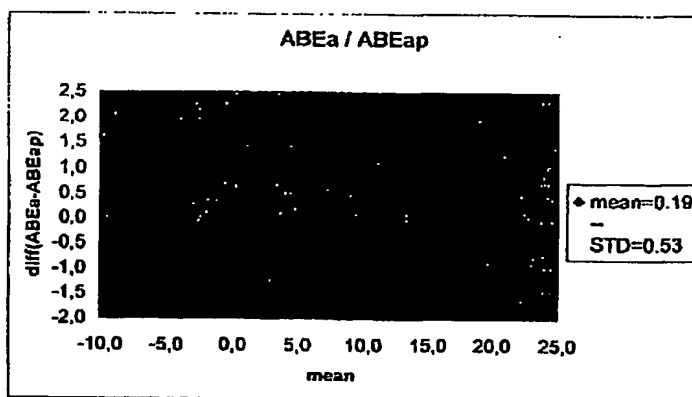


Fig. 8

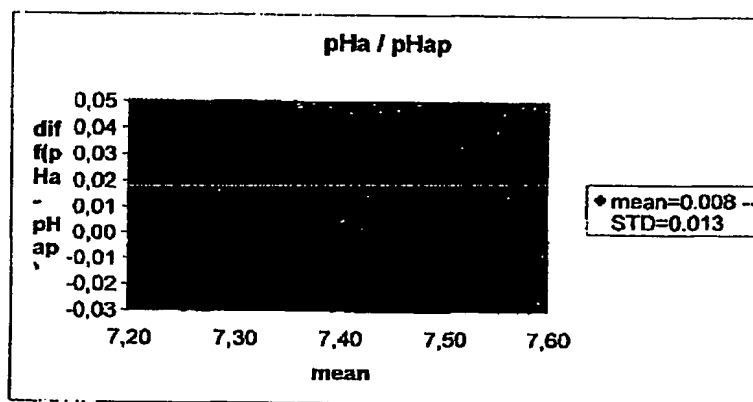


Fig. 9

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